CELLULOSE FIBRE BASED POLYMER COMPOSITES FOR APPLICATIONS IN DRUG DELIVERY

FINAL SYNOPSIS

OF THE PH.D. THESIS TO BE SUBMITTED

TO

THE FACULTY OF SCIENCE AND TECHNOLOGY OF

MANGALORE UNIVERSITY

FOR THE AWARD OF DEGREE OF

DOCTOR OF PHILOSOPHY

IN

CHEMISTRY

BY

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FEBRUARY 2024

Pre-Synopsis of the Ph.D. Thesis to be submitted to the Faculty of Science and Technology of Mangalore University

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Title of the Thesis:	**Cellulose fibre based polymer composites for applications in drug delivery.**
Registration Number:	**Ref: MU/EXB/Ph.D./CR.74/Chem./2020-21/E.13 dated 06-11-2020**
Date of Registration:	**28-03-2018**
Place of Work:	**Department of Post-Graduate Studies & Research in Chemistry** **Mangalore University** **Mangalgangothri-574199**

Introduction:

Nature in its own has so many resources and one such is a biopolymer, a polymer substance synthesised during the life span of plants, animals in the form of cellulose, starch etc. Among these, cellulose is the amplest biopolymer which is extensively used in food, pharmaceutic and biofuel sectors [1].

The abundant agricultural waste i.e. areca nut husk fibres are easily available, whose utilization needs more attention. The present study aims in the extraction of cellulose fibre from areca husk fibres [2]. Cellulose being the foremost constituent of a plant material is a polysaccharide consisting of a linear chain of several thousands of β(1→4) linked D-glucose units [3].

On the economic point of view, it is mainly preferred to produce fibres from locally available biomass waste to avoid high transport cost of raw material. In the recent years, the interest in the cellulose-based materials has been increasing due to demand for renewable resources and growing environmental awareness [4].

Cellulose fibre a biopolymer with astonishing properties has attained mammoth interest in drug delivery system. It is a biocompatible, biodegradable, easily available and nontoxic vehicle for the release of active drug molecules [5].

The natural polymers are preferred over synthetic polymers in biomedical applications because of their low cost, biodegradability, easy availability and non-toxicity. However, the natural polymers also possess certain drawbacks like uncontrolled hydration, drop in viscosity during storage etc [6]. By combing with synthetic polymers, the properties of these natural polymers can be easily modified. The chemical modification of natural and synthetic polymers results in a new material with desirable properties [7]. This modification can be easily brought by graft copolymerisation and formation of interpenetrating networks using N, N'-Dimethylacrylamide as a monomer [8].

The modification of cellulose fibre-based hydrogels was done by blending polymers or using clay and magnetic nanoparticles. Such typical fillers can be served as reinforcing agents to enhance the properties of hydrogels with various application [9,10,11].

Recently, the cellulose fibre-based hydrogel have been extensively investigated and widely used for biomedical applications such as drug encapsulation and delivery, tissue

engineering, biosensors etc. The cellulose fibre has gained much attention in the past few years because of their potential applications and can be used as component in the hydrogel as a matrix material for drug delivery [12,13,14].

After a thorough literature survey, it is observed that no much work has been reported on cellulose fibre as a component in hydrogel preparation. Hence, we have decided to explore their properties which might find some pharmaceutical applications.

The work presented in this thesis deals with the extraction, preparation, characterisation and application of the cellulose fibre-based hydrogels. CF wee extracted using alkalisation, bleaching and acid hydrolysis. The prepared CF were modified using another polysaccharide, monomer, initiator and the crosslinker [15].

The prepared hydrogels have been characterised by techniques such as FTIR, TGA, XRD, FESEM, EDS and VSM techniques. The swelling behaviour of the cellulose fibre-based hydrogel has been studied under different pH conditions. The swelling data has been analysed using different pH conditions and kinetic parameters of swelling have been evaluated. The applicability of the cellulose-based hydrogel has been explored. Drug release data has been analysed using available models such as zero-order, first order, Kosmeyer-Peppas and Higuchi model [16,17,18].

The result of work has been presented in the Thesis in five chapters as detailed below.

Chapter 1: General Introduction.

Chapter 2: Experimental Section.

Chapter 3: Polymer hydrogel from Cellulose fiber and DMA.

3.1.1: Preparation

3.1.2: Characterisation

3.1.3: Swelling Studies

3.1.4: Drug Release Study

Chapter 4: Polymer hydrogel from Cellulose fiber-Guar Gum and DMA.

4.1.1: Preparation

4.1.2: Characterisation

4.1.3: Swelling Studies

4.1.4: Drug Release Study

Chapter 5: Polymer hydrogel from Cellulose fiber and DMA incorporated with magnetic particle.

5.1.1: Preparation

5.1.2: Characterisation

5.1.3: Swelling Studies

5.1.4: Drug Release Study

Chapter 6: Polymer hydrogel from Cellulose fiber and DMA incorporated with clay particle.

6.1.1: Preparation

6.1.2: Characterisation

6.1.3: Swelling Studies

6.1.4: Drug Release Study

Chapter 7: Polymer hydrogel from Cellulose fiber-Pullulan and DMA.

7.1.1: Preparation

7.1.2: Characterisation

7.1.3: Swelling Studies

7.1.4: Drug Release Study

Summary and Conclusions

References

Chapter 1: General Introduction

This is an introductory part of the entire research work which includes the literature on areca cellulose fiber-based hydrogels.

Chapter 2: Experimental Sections:

Chapter 2 deals with experimental details of the synthesis and characterisation of polymers employed in the present study. This includes the preparation of cellulose fiber from areca cellulose and its use in the preparation of hydrogels by chemical and irradiation methods. The swelling ratio of the synthesised hydrogel have been discussed. The experimental details followed to determine the drug loading and its release studies are also presented. The details of the equipments used in the characterisation of polymers are also described. The various models used for kinetic analysis of data on swelling and drug release are described.

Chapter 3: Cellulose fiber-g-PDMA hydrogels.

This chapter describes the preparation, characterisation and applications of hydrogels composed of cellulose fiber-g-PDMA. The hydrogel of cellulose fiber and DMA was made by microwave irradiation of the aqueous solution of CF and DMA using the initiator (ammonium peroxodisulphate (APS) and N, N'-methylenebisacrylamide (MBA) as a crosslinker. The formation of hydrogel was confirmed by FTIR, TGA, XRD and FESEM analysis. The swelling properties such as initial swelling rate, swelling rate constant and the mechanism of water transport into the hydrogel were determined. The swelling were observed to be pH dependent. The ‘n’ value of the CF-g-PDMA under different pH conditions were in the range of 0.117-0.127, indicating the mechanism of water transport to be Fickian type. The suitability of the hydrogel as a matrix for the sustained release formulation of the drug Metformin Hydrochloride (MH) was studied. The drug release extent was found to be pH dependent. The MH release increased when the pH of the medium changed from 7.4 to 1.2. At pH 1.2, the hydrogel showed a maximum release of 95% at the end of 7 h and at pH 7.4, about 100% of the drug was release at the end of 12 h, indicating the suitability of the hydrogel CF-g-PDMA as the matrix material for the sustained release of the drug MH.

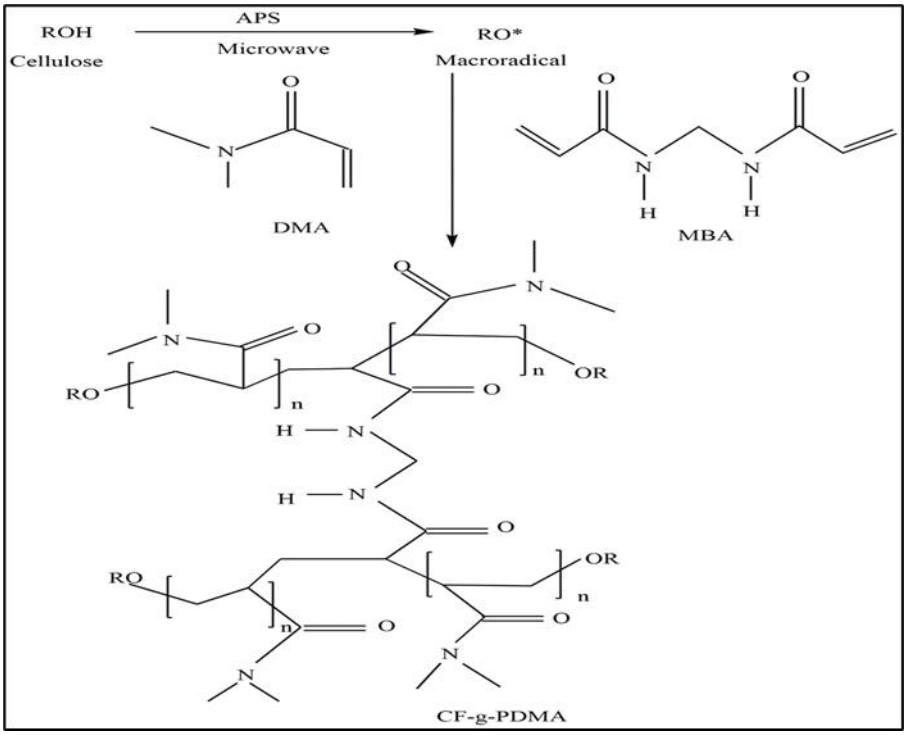

Fig. 1. Schematic representation of mechanism of formation of CF- g-PDMA gel.

Chapter 4: Cellulose fiber/Guar Gum-g-PDMA hydrogels.

The chapter described the formation of hydrogel of CF and Guar gum under microwave irradiation using DMA in the presence of initiator and crosslinker. The obtained hydrogel were confirmed by FTIR, TGA, XRD and FESEM techniques. The swelling properties such as initial swelling rate, swelling rate constant and the mechanism of water transport into the hydrogel were determined. The swelling is observed to be pH dependent. The suitability of the hydrogel for sustained release of the drug MH was increased when the pH of the medium was changed from 7.4 to 1.2. The results showed that the pH had no influence on the extent of drug release in the initial stages of release but towards the end the release appears to be slightly higher in medium of pH 1.2 and 100% release occurs at the end of 8 h in both pH media, indicating the suitability of the hydrogel as a matrix material for the release study of MH.

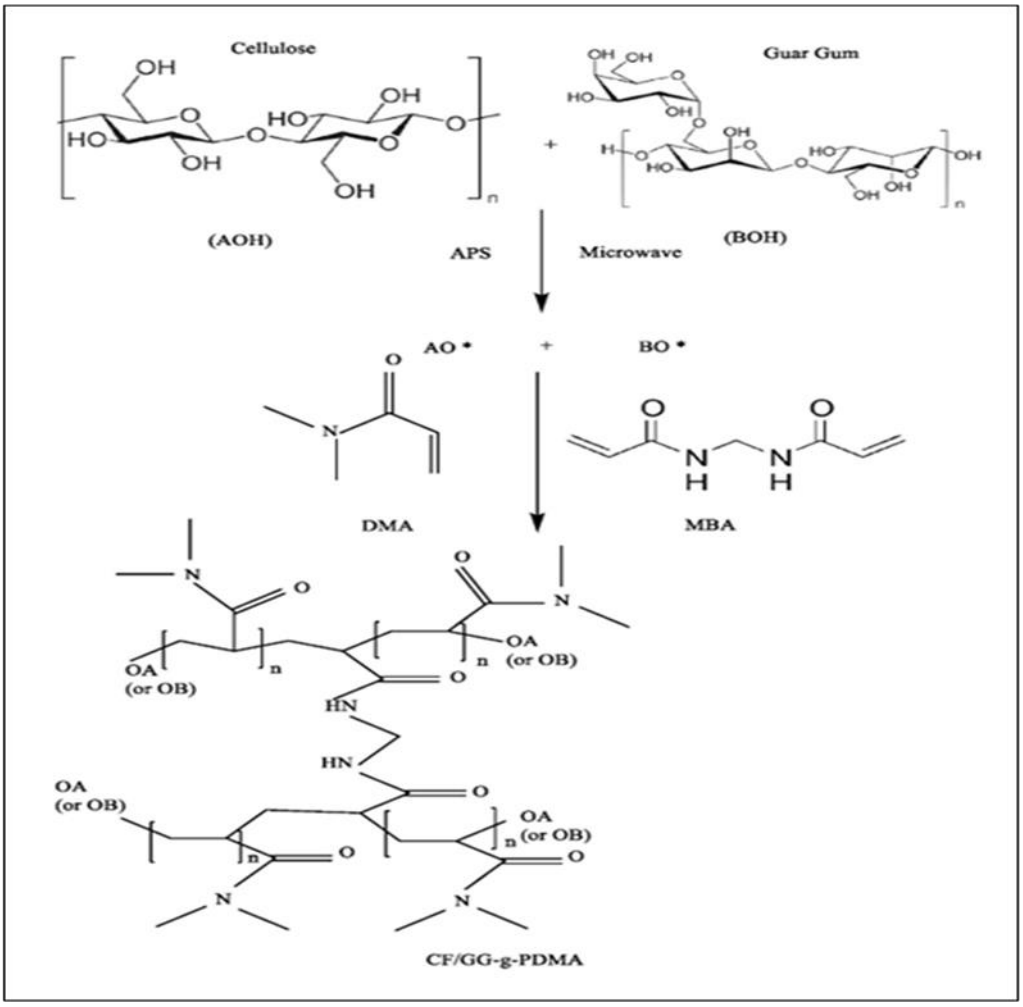

Fig. 2. Schematic representation of mechanism of formation of CF/GG-g-PDMA gel.

Chapter 5: Cellulose fiber-g-PDMA/ Fe_3O_4 hydrogels.

This chapter describes the formation of CF and DMA incorporated with magnetic particle. The hydrogel of cellulose fiber and DMA prepared under microwave irradiation using initiator and crosslinker was subjected to *in-situ* method. The magnetic particle incorporated hydrogel were confirmed by FTIR, TGA, XRD, FESEM, EDS and VSM techniques. The swelling is observed to be pH dependent with the 'n' value ranging from 0.17 to 0.20. The suitability of the hydrogel for the sustained release of the MH drug were studied under pH 1.2 and 7.4. At pH 7.4 about 90% of the drug was released and at pH 1.2, 100% of the drug was released showing the suitability of the hydrogel as a matrix for the drug release MH.

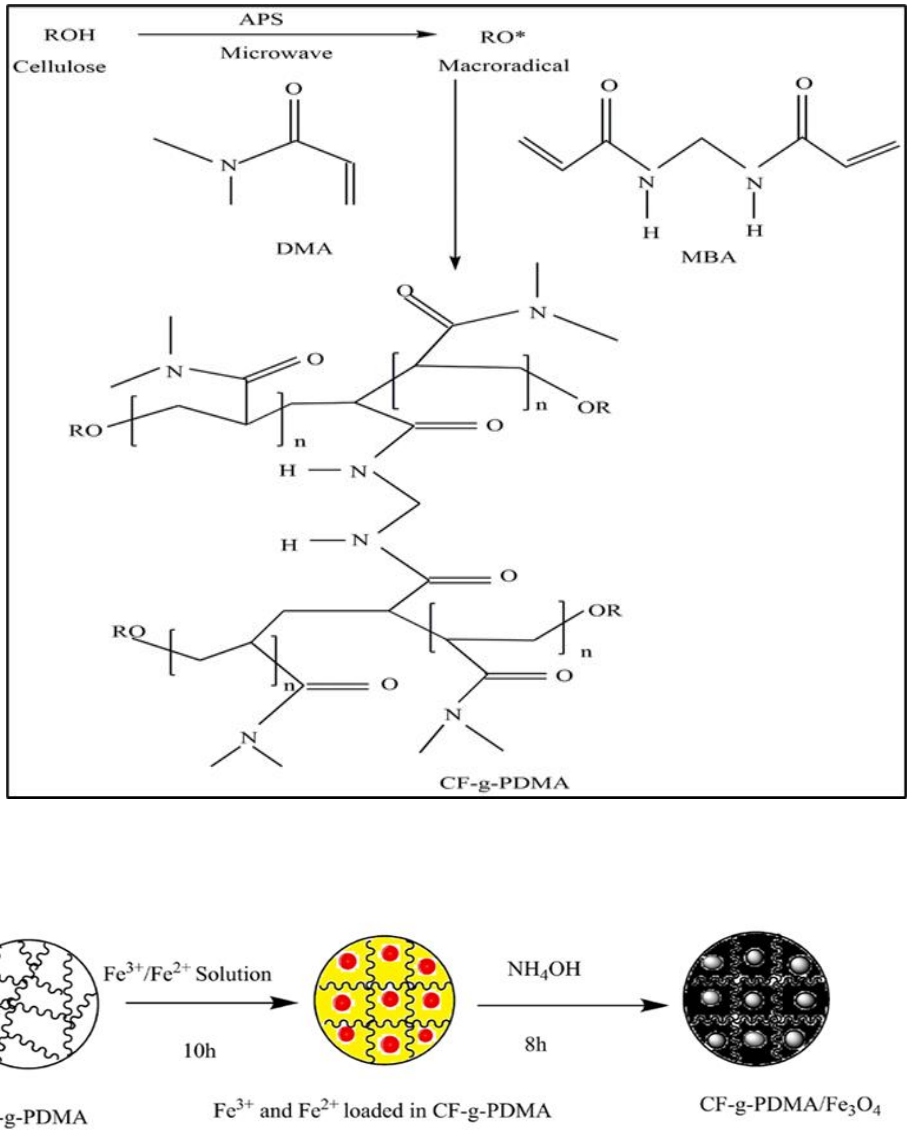

Fig. 3. Schematic representation of mechanism of formation of CF-g-PDMA/ Fe_3O_4 gel.

Chapter 5: Cellulose fiber-g-PDMA/MMT hydrogels.

This chapter describes the formation of hydrogel CF and DMA with the incorporation of clay particles. The clay particle incorporated hydrogel were confirmed by FTIR, TGA, XRD, FESEM and EDS techniques. The initial swelling rate, swelling rate constant and the mechanism of water transport were determined. The swelling is observed to be pH dependent with n value 0.4901 and 0.3607 and the mechanism to be non-Fickian and Fickian at pH 1.2 and 7.4. The suitability of the hydrogel for the sustained release of drug MH, were studied under pH 1.2 and 7.4 with 100% and 86% of the drug release at pH 1.2 and 7.4 indicating the suitability as a matrix for the drug release.

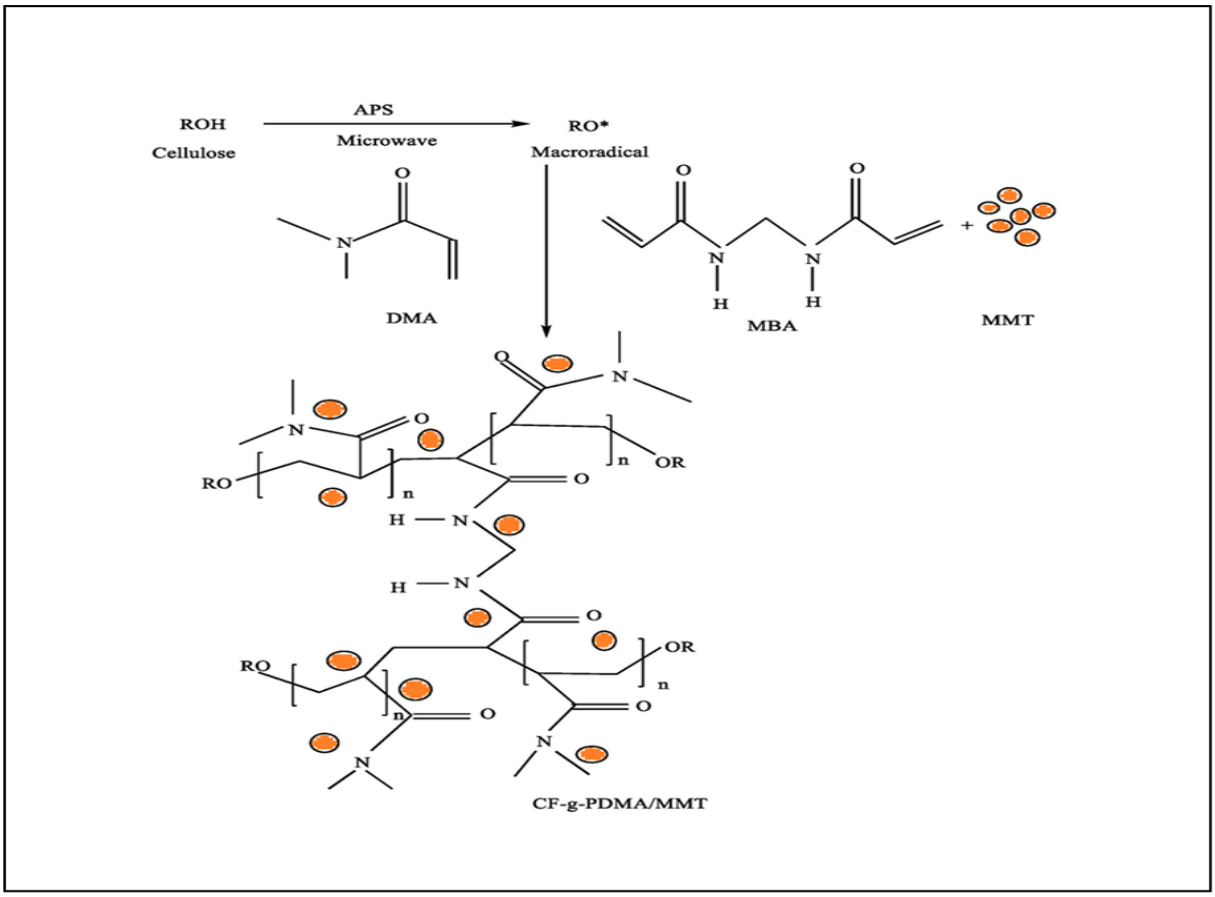

Fig. 4. Schematic representation of mechanism of formation of CF-g-PDMA/ MMT gel.

Chapter 5: Cellulose fiber/Pullulan-g-PDMA hydrogels.

This chapter describes the formation of hydrogel using CF and PL (Pullulan) under microwave irradiation using DMA in the presence initiator and crosslinker. The hydrogel were confirmed using FTIR, TGA, XRD and FESEM techniques. The swelling was performed and the properties such as initial swelling rate, swelling rate constant and the mechanism of water transport were analysed. The n value were in the range 0.36 and 0.23 for pH 1.2 and 7.4 indicating the mechanism to be Fickian. The hydrogel suitability as a matrix material for the drug release was carried out at two different pH. The MH release was observed to 95% at pH 1.2 and 100% at pH 7.4. The drug release studies indicating the suitability of the hydrogel as matrix material for the sustained release formulation of the drug MH.

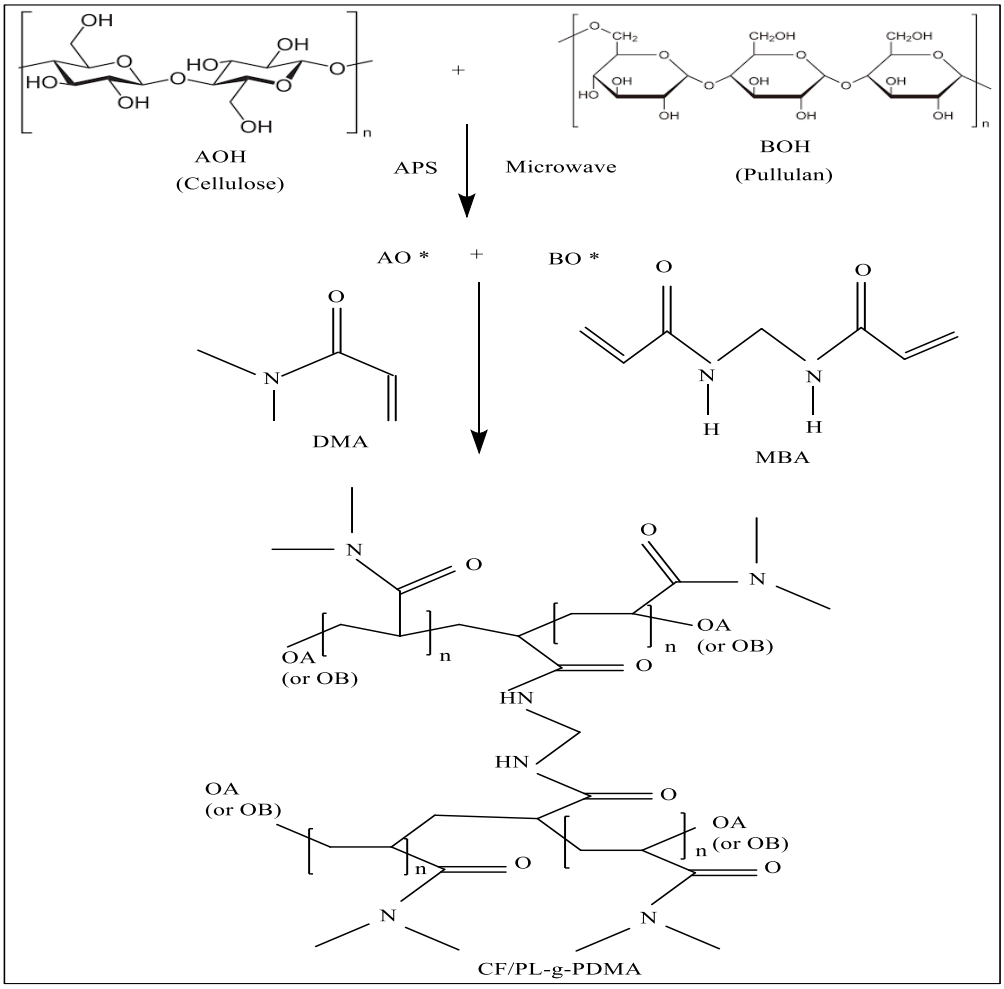

Fig. 5. Schematic representation of mechanism of formation of CF/PL-g-PDMA gel.

Summary and Conclusion:

A summary of the whole study is made and conclusion drawn based on the study are reported.

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List of publications:

1. **Smitha Rai,** Ruchira Raychaudhuri, Ritu Kudarha, Srinivas Mutalik, Vishalakshi B., Usha K. M., Bioderived Cellulose Fibre-Guar Gum Grafted Poly (N, N'-Dimethylacrylamide) Polymer Network for Controlled Release of Metformin Hydrochloride, International Journal of Biological Macromolecules 253 (2023)126882.

Paper under Communication:

1. **Smitha Rai**, Ruchira Raychaudhuri, Ritu Kudarha, Srinivas Mutalik, Vishalakshi B., Usha K. M., Hydrogels Based on Areca Cellulose Fibres for the Sustained Release of Metformin Hydrochloride (Polymer Bulletin).

Papers Presented in Conferences:

1. Presented a poster entitled "**Microwave Assisted Synthesis and Characterization of Areca Cellulose-g-Poly (N, N- dimethylacrylamide) Based Hydrogels**" in the

international conference on NANO VISION-2022 "Emerging Trends in Nanotechnology and Biotechnology" held on 19th and 20th April 2022 sponsored by DST-SERB, Govt of India organized by SGVU-Biotechnology Business Incubator (BBI) and school of Applied Science, Suresh Gyan Vihar University, Jaipur.

2. Oral presentation on "**Preparation and Characterization of Areca Cellulose-g-Poly (N, N- dimethylacrylamide) Hydrogels incorporated with Magnetic Nanoparticles**" in the international conference on RECENT TRENDS IN APPLIED SCIENCE (ICRTAS)-2022 held on 3rd and 4th August 2022 at Srinivas Institute of Technology, Valachil, Mangaluru.
3. Oral presentation on "**Bioderived Cellulose Fibre from Areca Husk as a potential material in hydrogel preparation**" in the international conference on "Recent Research in Applied Science "on 26th and 27th September 2023 held at Srinivas Institute of Technology, Valachil, Mangaluru **(Best Paper Award)**.

(Dr. Usha K. M.) (Smitha Rai)

Research Guide Research Student